

## **REMARKS AND ARGUMENTS**

Claims 17-29 are pending.

### **Amendments to the claims**

Claims 17, and 22 are currently amended to include the transitional language “comprising.” These amendments are supported in the specification at page 5, line 18 to page 6, line 9.

### **Claim Rejections – 35 U.S.C §103**

The determination of obviousness under 35 U.S.C. § 103(a) is based upon the factual inquiries set forth by the U.S. Supreme Court in *Graham v. John Deere*, 383 U.S. 1, 17-18. These factual inquiries are: determining the scope and content of the prior art; ascertaining the differences between the prior art and the claims in issue; resolving the level of ordinary skill in the pertinent art; and evaluating evidence of secondary considerations. *Id.* In formulating an obviousness rejection based upon a combination of prior art elements, it is necessary for the Office to identify a reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed. When performing this analysis,

[I]t will often be necessary to look to interrelated teachings of multiple patents; to the effect of demands known to the design community or present in the marketplace; and to the background knowledge possessed by a person having ordinary skill in the art. To facilitate review, this analysis should be made explicit.

*KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. \_\_\_, 127 S. Ct. 1727, 1740-41 (2007).

The Examiner has rejected claims 17-29 under 35 U.S.C §103(a) as unpatentable over Doerfler et al. (43 Neuroradiology 1112 (2001)) in view of Mottu et al. (21 Biomaterials 803 (2000)).

### **Scope and content of the prior art**

Doerfler et al. (43 Neuroradiology 1112 (2001)) teaches compositions of Lipiodol, an oily contrast medium, and Ethibloc®, an occlusion emulsion, for injection through a microcatheter, *in vitro*. Doerfler et al decreased the viscosity of Ethibloc by mixing with the oily contrast medium Lipiodol. Doerfler did not include

additional ethanol in the mixture, but rather varied the ratios of Ethibloc® and Lipiodol. The viscosity of the emulsions formed with only these two components does not fulfill the need for special applications in which the emulsion must be applied over a longer time-frame. (See instant application page 5 lines 4-10) The kit of the present invention allows adjustment of the viscosity without losing the radiopacity requirements for embolization. Further, Doerfler requires that the Ethibloc® be warmed to 37°C prior to mixing with the Lipiodol to achieve the mixture. (Doerfler at 1113, right-hand column). The kit of the present invention allows the preparation of stable emulsions without phase separation by mixing the Lipiodol with pure alcohol, because the three-syringe system allows the mixing of the components in such a manner so as to avoid warming the Ethibloc. (Application page 10 lines 13-19) In addition, while the “old mixture” of Ethibloc® and Lipiodol only separated even during application, the embolizate prepared by the method of the instant invention was stable for at least 2 hours. (Application page 10 lines 18-19 and 23-27) This is very convenient for use in an operating room, where extra steps in a procedure take time that can be disadvantageous to the patient. The Ethibloc®/Lipiodol only mixtures must be used in a short time. In complex procedures in the operating room which require more time for the manipulation, the two-component mixture is known to separate, resulting in a suspension rather than an emulsion, which can cause recanalization of the patient’s vascular sections, requiring repetition of the procedure. (Application page 3 line 29 – page 4 line 11) Therefore, the third component, extra ethanol, is important to make adjustments to the preparation of the emulsion for embolization for generating the right emulsion on-site for the procedure, as required. Also, Doerfler specifies the particular catheter to be used with each particular mixture. In an operating room scenario, this is not practical. It is far more efficient to have multiple catheters on hand and be able, by use of the kit of this invention, to adjust the viscosity and mixture of the embolization agent immediately prior to use, when a decision as to what is needed is made on-site in an operating room.

Mottu teaches water-miscible solvents for embolic liquids as shown in Table 2. (Mottu, page 805) Ethibloc® was not considered in the study because its properties in the presence of PBS (phosphate buffered saline), required for the test in that reference, were very unsatisfactory. (Id. page 806, left-hand column) In addition,

even in the systems tested, which did not include Ethibloc® as an embolizing agent, ethanol was considered the poorest solvent, causing precipitation of the polymers, and therefore ineffective for use in treating aneurysms, one of the vascular malformation for which embolization is used. (page 807, right-hand column) Therefore, the use of ethanol as a solvent for Ethibloc® and a radiopaque agent was not taught in Mottu, and the use of ethanol in the instant invention is not obvious based on Mottu, whether in view of Doerfler or not.

Given the state of the art in embolization emulsions at the time of the invention, it would not have been obvious to supply a kit of the type of the present invention. It was considered that dilution of the Ethibloc®/radiopaque agent mixture could form a suspension. (Application page 4, lines 1-2) The presence of air in a standard mix for use in a microcatheter is a danger to the patient which must be avoided. (Application page 4, lines 12-18) The use of the three-syringe kit of this invention avoids the problem of introduction of air into the system because it is closed. The ability to eliminate air from the emulsion by either vacuum or by centrifuging the syringe containing the final emulsion ensures that no air is available to cause problems in the catheterization process.

In sum, the kit of the present invention fulfills a need for the ability to adjust viscosity of embolization emulsions to suit the need of the patient on-site, is easier than a system that requires heating the components prior to mixing, and avoids problems of the presence of air in a catheter by being a closed and centrifugable system. Neither Doerfler, nor Mottu, together or singly, teach the preparation and use of a kit as in the present invention.

Applicant respectfully requests that the obviousness rejections be withdrawn based on the remarks set herein.

Applicants respectfully submit that the Examiner has not presented a case for *prima facie* obviousness. In view of the deficiencies, discussed above, of the cited prior art references, the instant invention is not “the results of ordinary innovation.”

*KSR International Co. v. Teleflex Inc. et al.*, 127 S.Ct. 1727, at 1746 (2007). The office Action fails to show a teaching or suggestion in the art to make the present claimed invention.

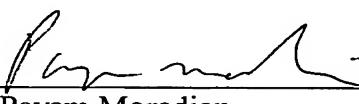
**Conclusion**

In view of the foregoing amendments and remarks, Applicant respectfully submits that the present application is in condition for allowance. Early and favorable action by the Examiner is earnestly solicited. If any outstanding issues remain, the examiner is invited to telephone the undersigned at the telephone number indicated below to discuss the same.

Respectfully submitted,

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By:



\_\_\_\_\_  
Payam Moradian  
Registration No. 52,048

KENYON & KENYON LLP  
One Broadway  
New York, New York 10004  
(212) 425-7200

**CUSTOMER NO. 26646**